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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/558,276	11/18/2005	Thomas Wisniewski	05986/100M536-US1	3691

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DARBY & DARBY P.C.
P.O. BOX 770
Church Street Station
New York, NY 10008-0770

EXAMINER	
BOESEN, AGNIESZKA	
ART UNIT	PAPER NUMBER
1648	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/558,276	WISNIEWSKI ET AL.	
	Examiner	Art Unit	
	AGNIESZKA BOESEN	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *26 April 2010*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3,4,9-13,15-20,22,23,28-31,33-37,40,45,46,51-53 and 56* is/are pending in the application.

4a) Of the above claim(s) *11-13, 15-19, 29-31, 33-37 and 40* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,3,4,9,10,20,22,23,28,45,46,51-53 and 56* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on April 26, 2010 has been entered.

Claims 1, 9, 10 and 20 have been amended. Claims 54-55 have been canceled. Rejections of canceled claims are moot. New claim 56 has been added. Claims 11-13, 15-19, 29-31, 33-37 and 40 are withdrawn because they are drawn to non-elected inventions. Claims 1, 3, 4, 9, 10, 20, 22, 23, 28, 45, 46, 51-53 and 56 are under consideration in this Office action.

This is a supplemental Office Action which restarts the time period for response.

Claim Rejections - 35 USC § 103

Rejection of Claim 1 under 35 U.S.C. 103(a) as being unpatentable over Bachmann et al. (Patent Application Publication No.: 2003/0219459 A1) in view of Gizurarson et al. (US Patent 6,514,503 B1) present in the Office action on 8/7/2008 **is withdrawn** in view of Applicant's arguments.

Rejection of Claims 9 and 56 under 35 U.S.C. 103(a) as being unpatentable over Bachmann et al. (Application Publication No.: 2003/0219459 A1) and Gizurarson et al. (US Patent 6,514,503 B1)as applied to claim 1 and further in view of Clemens et al. (US Patent 6,440,423 B1) and Kleanthous et al. (US Patent 6,585,975 B1) **is withdrawn** in view of Applicant's arguments.

Rejection of Claim 3 under 35 U.S.C. 103(a) as being unpatentable over Bachmann et al. (Patent Application Publication No.: 2003/0219459 A1) in view of Gizurarson et al. (US Patent 6,514,503 B1) and further in view of Peretz et al. (Nature 2001, Vol. 412, p. 739-743) and Kaneko et al. (JMB, 2000, Vol. 295, p. 997-1007) **is withdrawn** in view of Applicant's arguments.

Rejection of Claim 4 under 35 U.S.C. 103(a) as being unpatentable over Bachmann et al. (Patent Application Publication No.: 2003/0219459 A1) and Gizurarson et al. (US Patent 6,514,503 B1) as applied to claim 1 and further in view of Benkirane et al. (Journal of Biological Chemistry, 1993, Vol. 268, p. 26279-26285, in IDS of 11/18/2005) **is withdrawn** in view of Applicant's arguments.

Rejection of claim 9 under 35 U.S.C. 103(a) as being unpatentable over Bachmann et al. (Application Publication No.: 2003/0219459 A1) and Gizurarson et al. (US Patent 6,514,503 B1) as applied to claim 1 and further in view of Clemens et al. (US Patent 6,440,423 B1) and Kleanthous et al. (US Patent 6,585,975 B1) **is withdrawn** in view of Applicant's amendment.

Rejection of claim 10 under 35 U.S.C. 103(a) as being unpatentable over Bachmann et al. (Application Publication No.: 2003/0219459 A1) and Gizurarson et al. (US Patent 6,514,503 B1)as applied to claim 1 and further in view of Clemens et al. (US Patent 6,440,423 B1) and Kleanthous et al. (US Patent 6,585,975 B1) **is withdrawn** in view of Applicant's arguments.

Rejection of Claims 20, 22 and 28 under 35 U.S.C. 103(a) as being unpatentable over Bachmann et al. (Patent Application Publication No.: 2003/0219459 A1), Gizurarson et al. (US Patent 6,514,503 B1) and Lu et al. (US Patent 5,733,760) and further in view of Chabalgoity et

al. (Vaccine, 2001, Vol. 19, p. 460-469, in IDS of 11/18/2005) **is withdrawn** in view of Applicant's arguments.

Rejection of Claims 23 and 46 under 35 U.S.C. 103(a) as being unpatentable over Bachmann et al. (Patent Application Publication No.: 2003/0219459 A1), Gizurarson et al. (US Patent 6,514,503 B1) and Lu et al. (US Patent 5,733,760) as applied to claims 22 and further in view of Benkirane et al. (Journal of Biological Chemistry, 1993, Vol. 268, p. 26279-26285) **is withdrawn** in view of Applicant's arguments.

Rejection of Claim 45 under 35 U.S.C. 103(a) as being unpatentable over Bachmann et al. (Patent Application Publication No.: 2003/0219459 A1), Gizurarson et al. (US Patent 6,514,503 B1) and Lu et al. (US Patent 5,733,760) and Chabalgoity et al. (Vaccine, 2001, Vol. 19, p. 460-469, in IDS of 11/18/2005) further in view of Peretz et al. (Nature 2001, Vol. 412, p. 739-743) and Kaneko et al. (JMB, 2000, Vol. 295, p. 997-1007) **is withdrawn** in view of Applicant's arguments.

Rejection of Claims 51 -53 under 35 U.S.C. 103(a) as being unpatentable over Bachmann et al. (Patent Application Publication No.: 2003/0219459 A1), Gizurarson et al. (US Patent 6,514,503 B1) and Lu et al. (US Patent 5,733,760), Kotloff (Infection and Immunity, 2002, Vol. 70, p. 2016-2021) and further in view of Chabalgoity et al. (Vaccine, 2001, Vol. 19, p. 460-469, in IDS of 11/18/2005) Lu et al. (US Patent 5,733,760) Benkirane et al. (Journal of Biological Chemistry, 1993, Vol. 268, p. 26279-26285) Peretz et al. (Nature 2001, Vol. 412, p. 739-743) and Kaneko et al. (JMB, 2000, Vol. 295, p. 997-1007) **is withdrawn** in view of Applicant's arguments.

New Rejections

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claim 1 is rejected under 35 U.S.C. 102(a) as being anticipated by Sigurdsson et al. (American Journal of Immunology, 2002, Vol. 161, p. 13-17).

Sigurdsson discloses a composition comprising an isolated non-infectious, non-pathogenic mouse prion protein (see the entire document, particularly Figure 1A). The composition is suitable for mucosal administration and it induces Th-2 type associated antibody immune responses.

Thus by this disclosure Sigurdsson anticipates the present claims.

Claim 1 is rejected under 35 U.S.C. 102(b) as being anticipated by Williamson et al. (PNAS, 1996, Vol. 93, p. 7279-7282).

Williamson discloses compositions an isolated non-infectious, non-pathogenic mouse prion protein (see Materials and Methods). The composition is suitable for mucosal administration and it induces Th-2 type associated antibody immune responses.

Thus by this disclosure Sigurdsson anticipates the present claims.

Claim 1 is rejected under 35 U.S.C. 102(b) as being anticipated by Prusiner et al. (US Patent 6,290,954 B1).

Prusiner discloses compositions an isolated non-infectious, non-pathogenic mouse prion protein (see Examples 2 and 3). The composition is suitable for mucosal administration and it induces Th-2 type associated antibody immune responses.

Thus by this disclosure Prusiner anticipates the present claims.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 20, 28, 51 and 52 are rejected under 35 U.S.C. 103(a) as being unpatentable over Sigurdsson et al. (American Journal of Immunology, 2002, Vol. 161, p. 13-17) in alternative with Prusiner et al. (US Patent 6,290,954) and in alternative with Williamson et al. (PNAS, 1996, Vol. 93, p. 7279-7282) in view of Lu et al. (US Patent 5,733,760) and Chabalgoity et al. (Vaccine, 2001, Vol. 19, p. 460-469, in IDS of 11/18/2005) and Grones (Biochemical and Biophysical Research Communications, 1995, Vol. 206, p. 942-947).

Sigurdsson, Williamson and Prusiner teach a composition comprising isolated non-infectious, non-pathogenic mouse prion protein. Neither Sigurdsson, Williamson nor Prusiner teach Shigella or Salmonella transformed with a vector expressing non-infectious, non-pathogenic mouse prion protein.

Lu et al. teach vaccine compositions comprising attenuated *Salmonella* vectors expressing heterologous DNA encoding viral antigens from HIV and HCV viruses (see the entire

document, particularly claims 1-9, column 5, lines 65-67, column 10, lines 19-60). While Lu et al. teach *Salmonella typhi, Salmonella typhimurium, and Salmonella enteritidis*, (see column 6, lines 65-67, Lu et al. does not teach the specific *Salmonella* strains as recited in the present claim 28.

Chabalgoity et al. teach *Salmonella typhimurium* LVR01 strain expressing heterologous antigens encoding binding fatty acid protein from *Echinococcus granulosus* (see the entire document, particularly Materials and Methods).

Grones teaches Shigella transformed with heterologous plasmids (see Results and Discussion).

It would have been *prima facie* obvious to express Sigurdsson's, Williamson's or Prusiner's mouse prion protein in Lu's and Chabalgoity *Salmonella* bacterial vectors used for expression of heterologous antigens and to provide a composition comprising attenuated *Salmonella typhi* bacterium transfected spp strain transformed with a vector capable of expressing a mammalian prion protein.

One would have been motivated to express Sigurdsson's, Williamson's or Prusiner's mouse prion protein in Lu's attenuated *Salmonella* or in Grones' *Shigella* because Lu et al. teach that their *Salmonella* vectors are particularly effective for induction of mucosal protective immune responses against mucosally transmitted infectious agents. Lu et al. also teach that attenuated Salmonella vectors are effective vectors for delivery of desired antigens because the bacteria grow rapidly and do not require growth in cell culture, thus allowing large scale production of vectors (see column 1, lines 19-55).

One would have been motivated to use Chabalgoity's *Salmonella typhimurium* LVR01 because Chabalgoity et al. teach that heterologous antigens expressed in LVR01 effectively elicits humoral and cellular immune responses in animals (see the entire document, particularly Results and Discussion on page 468).

One would have had a reasonable expectation of success to provide a composition comprising an attenuated *Salmonella typhi* bacterium and particularly *Salmonella typhimurium* LVR01 transformed with a vector capable of expressing a mammalian prion protein because the technology used for generation of bacterial recombinant vectors has been available to the skilled artisan at the time of the present invention. Moreover, the bacterial recombinant vectors expressing heterologous antigens have been successfully made in the art at the time of the invention as evidenced by Lu et al. and Chabalgoity et al.

Therefore, the invention as a whole would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made.

Claims 3, 4, 22, 23 and 53 are rejected under 35 U.S.C. 103(a) as being unpatentable over Sigurdsson et al. (American Journal of Immunology, 2002, Vol. 161, p. 13-17) in alternative with Prusiner et al. (US Patent 6,290,954) and in alternative with Williamson et al. (PNAS, 1996, Vol. 93, p. 7279-7282) as applied to claims 1 and 20 in view of Lu et al. (US Patent 5,733,760) and Chabalgoity et al. (Vaccine, 2001, Vol. 19, p. 460-469, in IDS of 11/18/2005) and further in view of Dunne et al. (US Patent Application Publication 2002/0194634 A1) and Benkirane et al. (Journal of Biological Chemistry, 1993, Vol. 268, p. 26279-26285, in IDS of 11/18/2005).

Sigurdsson, Williamson and Prusiner teach a composition comprising isolated non-infectious, non-pathogenic mouse prion protein. Neither Sigurdsson, Williamson nor Prusiner teach SEQ ID NO: 4 or D-amino acids.

Dunne teaches present SEQ ID NO: 4 (see SEQ ID NO: 10).

Benkirane et al. teach that changing the amino acids within an antigenic peptide from an L-residue to the corresponding D-residue drastically increases the antigenicity of the peptide and contributes to the generation of high levels of IgG3 antibodies in immunized animals (see the entire document, particularly page 26279 and Discussion).

Thus based on the teaching of Benkirane et al., it would have been *prima facie* obvious to the person skilled in the art to provide a pharmaceutical composition designed for induction of immune responses, wherein the amino acids within the antigenic protein are D-amino acids. It would have been *prima facie* obvious to the person skilled in the art to provide a pharmaceutical composition comprising Dunnes' s SEQ ID NO: 4 representing deer prion protein.

One would have been motivated to provide Sigurdsson, Williamson or Prusiner's pharmaceutical composition comprising mammalian prion protein wherein the amino acids of the prion protein are D-amino acids, because Benkrine et al. teach that changing the amino acids within an antigenic peptide from L- to D- amino acids results in increased antigenicity and thus better immunogenicity of the peptide.

One would have had a reasonable expectation of success to provide a composition comprising a mammalian prion protein wherein all amino acids are D-amino acids, because the means required for the synthesis of proteins containing D-amino acid residues have been

available to the skilled artisan at the time of the present invention as evidenced by Benkriane et al.

Therefore, the invention as a whole would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made.

Claims 9, 10 and 56 are rejected under 35 U.S.C. 103(a) as being unpatentable over Sigurdsson et al. (American Journal of Immunology, 2002, Vol. 161, p. 13-17) in alternative with Prusiner et al. (US Patent 6,290,954) and in alternative with Williamson et al. (PNAS, 1996, Vol. 93, p. 7279-7282) in view of Lu et al. (US Patent 5,733,760) and Chabalgoity et al. (Vaccine, 2001, Vol. 19, p. 460-469, in IDS of 11/18/2005) in view of Clemens et al. (US Patent 6,440,423 B1) and Kleanthous et al. (US Patent 6,585,975 B1).

Sigurdsson, Williamson and Prusiner teach a composition comprising isolated non-infectious, non-pathogenic mouse prion protein. Neither Sigurdsson, Williamson nor Prusiner teach the composition wherein the prion protein is covalently attached to the cholera toxin subunit B or aluminum hydroxide as a delivery vehicle.

Clemens et al. teach cholera toxin subunit B as an effective adjuvant comprised in vaccine compositions comprising viral or bacterial antigens (see the entire document, particularly claims 1-7 and column 4, lines 28-51). It is noted that Clemens et al. also teach another adjuvant species recited in claim 9, the heat-liable enterotoxin (LT) (see column 9, lines 60-67 and column 10, lines 1-67). Clemens et al. do not expressly teach covalent attachment of cholera toxin subunit B to the antigenic protein.

Kleanthous et al. teach covalent attachment of cholera toxin subunit B adjuvant to the antigenic protein (column 5, lines 1-20). Kleanthous et al. teach adjuvant aluminum hydroxide (see column 6, lines 3-8).

It would have been *prima facie* obvious to covalently attach cholera toxin subunit B to the prion protein. One would have been motivated to covalently attach Clemens' cholera toxin subunit B to Sigurdsson, Williamson or Prusiner 's prion protein, because Clemens' teach that cholera toxin subunit B adjuvant allows for improved mode of oral immunization and development of serum and mucosal antibodies against pathogenic microorganisms and that the cholera toxin subunit B is useful in combination with any specific antigen where a specific neutralizing antibody response would be beneficial in ablating the disease state associated with the antigen (see column 9, lines 5-26).

One would have had a reasonable expectation of success to provide a pharmaceutical composition comprising prion protein covalently attached to the cholera toxin subunit B, because a covalent attachment of cholera toxin subunit B to antigens of interest has been successfully practiced in the art as evidenced by Kleanthous et al.

Therefore, the invention as a whole would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made.

Conclusion

No claim is allowed.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Zachariah Lucas can be reached on 571-272-0905. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Agnieszka Boesen/
Examiner, Art Unit 1648